REMARKS

Claims 1-11, 16, 18-21, 24, 25 and 30-32 are pending in the instant application. Claims 3, 8, 9, 16, 18-21, 24, 25 and 30-32 have been withdrawn from consideration by the Examiner. Claims 1, 2, 4-7, 10 and 11 have been rejected. Claim 10 has been amended. New claims 36-39 have been added. Support for these amendments is provided in the specification at page 4, lines 11-15 and lines 22-23, and page 21 lines 7-11. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Finality of Election/Restrictions

The Restriction Requirement mailed October 31, 2007 has been made final. The Examiner has withdrawn claims 3, 8-9, 16, 18-21, 24-25 and 30-32 as being drawn to a nonelected invention/species. The traversal based upon Packard not teaching Lp-PLA2 and CRP in combination synergistically predicting risk of coronary events was not found convincing as the claims do not recite this feature. Applicants disagree as the feature of measuring **both** Lp-PLA2 and CRP in the patient is clearly stated in the claims. As discussed in more detail in Section IV, Packard does not teach this limitation. The unexpected result achieved by such measurement and evidenced by results set forth in the specification for example at pages 32-33 need not be

specifically recited in the claim. See MPEP 2145. Accordingly rejoinder of claims restricted based upon teachings of Packard is respectfully requested.

Further, with respect to finality of the species election, it is respectfully pointed out that the claims should only be restricted to this species if no generic claim is held allowable. See MPEP § 809.01 and 37 CF.R. § 1.146. Arguments set forth in Sections IV and V make clear that the generic claim is allowable over the cited art. Accordingly, searching of additional species is respectfully requested.

II. Objection to Specification

The specification has been objected to for use of trademarks such as ALEXA FLUOR® 350 which are not capitalized and not accompanied by the generic terminology. Accordingly, the specification has been amended to capitalize trademarks and to include generic terminology.

Withdrawal of this objection is respectfully requested.

III. Objection to Claim 10

Claim 10 has been objected to for use of the abbreviation ATP III. Accordingly, in an earnest effort to advance the prosecution of this case and in accordance with

teachings at page 4, line 22-23, Applicants have amended claim 10 to state Adult Treatment Panel III.

IV. Rejection of Claims 1, 2, 4-7 and 11 under 35 U.S.C. 102(b)

Claims 1, 2, 4-7 and 11 have been rejected under 35 U.S.C. 102(b) as being anticipated by Packard et al. (NEJM 2000 343:1148-1155). The Examiner suggests that Packard teach the limitations of claim 1 including measuring levels of Lp-PLA2 and CRP (page 1149 'measurements' section 2nd paragraph), analyzing the risks (Table 5), and using the risks (page 1152 'discussion' section 1st paragraph, Table 5) thus meeting the limitations of claim 1 of the instant invention.

Applicants respectfully traverse this rejection.

In the Office Action dated 5/15/08, the Examiner states:

> Packard specifically teach a multivariate assessment on the risk of a coronary event (Table 5). As such, the models used the variables including CRP and Lp-PLA2 (i.e. a combination of risk factors). Packard confirms that CRP and Lp-PLA2 are both indicators of risk of coronary heart disease (page 1152 'discussion' section 1st paragraph).

The Examiner then concludes that "taken together, Packard teach the limitations of claim 1 including measuring levels of Lp-PLA2 and CRP (page 1149 "measurements section

2nd paragraph), analyzing the risks (Table 5), and using the risks (page 1152 'discussion' section 1st paragraph, Table 5)."

Applicants respectfully disagree with the Examiner's interpretation and characterization of the teachings of Packard.

Contrary to the Examiner's suggestion, Packard clearly teaches that Lp-PLA2 is an **independent** [emphasis added] predictor of coronary heart disease, not part of a multivariate assessment on the risk of a coronary event.

Specifically, in the "Statistical Analysis" section of the Methods on page 1149, Packard states "We used multivariate conditional logistic-regression models to assess the **independent** [emphasis added] prognostic value of variables."

Further, in the "Results" section at the first full paragraph in column 2 at page 1150 Packard states: "The **independence** [emphasis added] of these variables as predictors of coronary events was assessed, as shown in Table 5 and Figure 1."

Finally in the last paragraph of the discussion Packard concludes from their study that "C-reactive protein, fibrinogen and the white cell count are interrelated markers

. . ." while Lp-PLA2 is concluded to be "a potential risk factor that may have a direct role in atherogenesis."

Accordingly, Packard, when read in its entirety is quite clear; multivariate assessment of variables (Lp-PLA2, CRP, etc.) was to determine independence of the variables, and not as "a multivariate assessment on the risk of a coronary event" or "a combination of [CRP and Lp-PLA2] risk factors" as suggested by the Examiner. Packard in no way teaches use of the combined risks of Lp-PLA2 and CRP to assess the risk of CVD in a patient as claimed. Accordingly, since Packard does not teach all elements of the instant claimed invention, this reference cannot anticipate the claimed invention. See MPEMP 2131.

Withdrawal of this rejection under 35 U.S.C. 102(b) is respectfully requested.

V. Rejection of Claims 1, 2, 4-7 and 10-11 under 35 U.S.C. 103(a)

Claims 1-2, 4-7 and 10-11 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Packard et al. (NEJM 2000 343:1148-1155) and further in view of Rao et al. (US 2003/0120134). The Examiner suggests that both Packard and Rao teach methods for assessing risk of coronary heart disease. Further, the Examiner suggests that since there is evidence that cardiovascular risk and disease is under-

treated, one would be motivated to use various methods and combinations of methods to assess risk of coronary heart disease. The Examiner suggests that in particular one would be motivated to use the CRP and Lp-PLA2 risks and additionally use the ATP III guidelines as taught by Rao with the method of Packard thus meeting the limitations of the claims of the invention.

Applicants respectfully traverse this rejection.

Claims of the instant application are drawn to methods and kits for assessing risk of Coronary Vascular Disease (CVD) in a patient which comprise measuring levels of both Lipoprotein Associated Phospholipase A2 (Lp-PLA2) and C-reactive protein (CRP) or Low Density Lipoprotein Cholesterol (LDL) in the patient, analyzing a risk associated with the level of CRP or LDL and a risk associated with the level of Lp-PLA2, and **using the combined risks** to assess the risk of CVD in the patient.

The cited combination of Packard and Rao does not teach or suggest using the combined risks of CRP or LDL and Lp-PLA2 to assess the risk of CVD in a patient as claimed.

Instead, as discussed in Section IV, supra, Packard assessed the **independent** [emphasis added] prognostic value of variables including CRP and Lp-PLA2 and concluded "C-reactive protein, fibrinogen and the white cell count are interrelated markers . . ." while Lp-PLA2 is concluded to be

"a potential risk factor that may have a direct role in atherogenesis."

Rao et al. fails to remedy deficiencies in Packard as this reference provides no teaching whatsoever with respect to measuring either Lp-PLA2 or CRP.

Thus, the cited combination of references does not teach or suggest all limitations of the claims and cannot render obvious the instant claimed invention.

Further, MPEP 2141 in citing the KSR decision states: "When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established function." KSR v. Teleflex 82 USPQ2d at 1396".

Clearly, the instant claimed invention drawn to using the combined risks of CRP and Lp-PLA2 to assess the risk of CVD in a patient evidenced in the specification for the first time to be complimentary markers of CHD risk and patients is an improvement of more than any predictable use set forth by Packard and Rao.

Accordingly, the combination Packard and Rao, which do not teach or suggest all the claim limitations and for not predict the improvements in the methods and kits of the present invention in assessing the risk of CVD, do not render obvious the instant claimed invention.

Withdrawal of this rejection under 35 U.S.C. 103(a) is therefore respectfully requested.

VI. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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